

# SEQUENCE LISTING

## (1) GENERAL INFORMATION:

- (i) APPLICANT: ST. GEORGE-HYSLOP, PETER H  
ROMMENS, JOHANNA M  
FRASER, PAUL E
- (ii) TITLE OF INVENTION: GENETIC SEQUENCES AND PROTEINS RELATED  
TO ALZHEIMER'S DISEASE AND USES THEREFOR.
- (iii) NUMBER OF SEQUENCES: 2
- (iv) CORRESPONDENCE ADDRESS:  
(A) ADDRESSEE: LERNER, DAVID, LITTENBERG, KRUMHOLZ &  
MENTLIK  
(B) STREET: 600 SOUTH AVENUE WEST  
(C) CITY: WESTFIELD  
(D) STATE: NJ  
(E) COUNTRY: USA  
(F) ZIP: 07090-1497
- (v) COMPUTER READABLE FORM:  
(A) MEDIUM TYPE: Floppy disk  
(B) COMPUTER: IBM PC compatible  
(C) OPERATING SYSTEM: PC-DOS/MS-DOS  
(D) SOFTWARE: ASCII
- (vi) CURRENT APPLICATION DATA:  
(A) APPLICATION NUMBER:  
(B) FILING DATE:  
(C) CLASSIFICATION:
- (viii) ATTORNEY/AGENT INFORMATION:  
(A) NAME: PALISI, THOMAS M  
(B) REGISTRATION NUMBER: 36,629  
(C) REFERENCE/DOCKET NUMBER: SCHERING 3.0-033
- (ix) TELECOMMUNICATION INFORMATION:  
(A) TELEPHONE: (908) 654-5000  
(B) TELEFAX: (908) 654-7866

## (2) INFORMATION FOR SEQ ID NO:1:

- (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 467 amino acids  
(B) TYPE: amino acid  
(D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:
- ```

Met Thr Glu Leu Pro Ala Pro Leu Ser Tyr Phe Gln Asn Ala Gln Met
 1                      5                      10                      15

Ser Glu Asp Asn His Leu Ser Asn Thr Val Arg Ser Gln Asn Asp Asn
                20                      25                      30

Arg Glu Arg Gln Glu His Asn Asp Arg Arg Ser Leu Gly His Pro Glu
 35                      40                      45
  
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Pro Leu Ser Asn Gly Arg Pro Gln Gly Asn Ser Arg Gln Val Val Glu  
 50 55 60  
 Gln Asp Glu Glu Glu Asp Glu Glu Leu Thr Leu Lys Tyr Gly Ala Lys  
 65 70 75 80  
 His Val Ile Met Leu Phe Val Pro Val Thr Leu Cys Met Val Val Val  
 85 90 95  
 Val Ala Thr Ile Lys Ser Val Ser Phe Tyr Thr Arg Lys Asp Gly Gln  
 100 105 110  
 Leu Ile Tyr Thr Pro Phe Thr Glu Asp Thr Glu Thr Val Gly Gln Arg  
 115 120 125  
 Ala Leu His Ser Ile Leu Asn Ala Ala Ile Met Ile Ser Val Ile Val  
 130 135 140  
 Val Met Thr Ile Leu Leu Val Val Leu Tyr Lys Tyr Arg Cys Tyr Lys  
 145 150 155 160  
 Val Ile His Ala Trp Leu Ile Ile Ser Ser Leu Leu Leu Leu Phe Phe  
 165 170 175  
 Phe Ser Phe Ile Tyr Leu Gly Glu Val Phe Lys Thr Tyr Asn Val Ala  
 180 185 190  
 Val Asp Tyr Ile Thr Val Ala Leu Leu Ile Trp Asn Phe Gly Val Val  
 195 200 205  
 Gly Met Ile Ser Ile His Trp Lys Gly Pro Leu Arg Leu Gln Gln Ala  
 210 215 220  
 Tyr Leu Ile Met Ile Ser Ala Leu Met Ala Leu Val Phe Ile Lys Tyr  
 225 230 235 240  
 Leu Pro Glu Trp Thr Ala Trp Leu Ile Leu Ala Val Ile Ser Val Tyr  
 245 250 255  
 Asp Leu Val Ala Val Leu Cys Pro Lys Gly Pro Leu Arg Met Leu Val  
 260 265 270  
 Glu Thr Ala Gln Glu Arg Asn Glu Thr Leu Phe Pro Ala Leu Ile Tyr  
 275 280 285  
 Ser Ser Thr Met Val Trp Leu Val Asn Met Ala Glu Gly Asp Pro Glu  
 290 295 300  
 Ala Gln Arg Arg Val Ser Lys Asn Ser Lys Tyr Asn Ala Glu Ser Thr  
 305 310 315 320  
 Glu Arg Glu Ser Gln Asp Thr Val Ala Glu Asn Asp Asp Gly Gly Phe  
 325 330 335  
 Ser Glu Glu Trp Glu Ala Gln Arg Asp Ser His Leu Gly Pro His Arg  
 340 345 350  
 Ser Thr Pro Glu Ser Arg Ala Ala Val Gln Glu Leu Ser Ser Ser Ile  
 355 360 365  
 Leu Ala Gly Glu Asp Pro Glu Glu Arg Gly Val Lys Leu Gly Leu Gly  
 370 375 380

Asp Phe Ile Phe Tyr Ser Val Leu Val Gly Lys Ala Ser Ala Thr Ala  
 385 390 395 400  
 Ser Gly Asp Trp Asn Thr Thr Ile Ala Cys Phe Val Ala Ile Leu Ile  
 405 410 415  
 Gly Leu Cys Leu Thr Leu Leu Leu Leu Ala Ile Phe Lys Lys Ala Leu  
 420 425 430  
 Pro Ala Leu Pro Ile Ser Ile Thr Phe Gly Leu Val Phe Tyr Phe Ala  
 435 440 445  
 Thr Asp Tyr Leu Val Gln Pro Phe Met Asp Gln Leu Ala Phe His Gln  
 450 455 460  
 Phe Tyr Ile  
 465

(2) INFORMATION FOR SEQ ID NO:2:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 449 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Met Leu Thr Phe Met Ala Ser Asp Ser Glu Glu Glu Val Cys Asp Glu  
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 Arg Thr Ser Leu Met Ser Ala Glu Ser Pro Thr Pro Arg Ser Cys Gln  
 20 25 30  
 Glu Gly Arg Gln Gly Pro Glu Asp Gly Glu Asn Thr Ala Gln Trp Arg  
 35 40 45  
 Ser Gln Glu Asn Glu Glu Asp Gly Glu Glu Asp Pro Asp Arg Tyr Val  
 50 55 60  
 Cys Ser Gly Val Pro Gly Arg Pro Pro Gly Leu Glu Glu Glu Leu Thr  
 65 70 75 80  
 Leu Lys Tyr Gly Ala Lys His Val Ile Met Leu Phe Val Pro Val Thr  
 85 90 95  
 Leu Cys Met Ile Val Val Val Ala Thr Ile Lys Ser Val Arg Phe Tyr  
 100 105 110  
 Thr Glu Lys Asn Gly Gln Leu Ile Tyr Thr Pro Phe Thr Glu Asp Thr  
 115 120 125  
 Pro Ser Val Gly Gln Arg Leu Leu Asn Ser Val Leu Asn Thr Leu Ile  
 130 135 140  
 Met Ile Ser Val Ile Val Val Met Thr Ile Phe Leu Val Val Leu Tyr  
 145 150 155 160  
 Lys Tyr Arg Cys Tyr Lys Phe Ile His Gly Trp Leu Ile Met Ser Ser  
 165 170 175

Leu Met Leu Leu Phe Leu Phe Thr Tyr Ile Tyr Leu Gly Glu Val Leu  
 180 185 190  
 Lys Thr Tyr Asn Val Ala Met Asp Tyr Pro Thr Leu Leu Leu Thr Val  
 195 200 205  
 Trp Asn Phe Gly Ala Val Gly Met Val Cys Ile His Trp Lys Gly Pro  
 210 215 220  
 Leu Val Leu Gln Gln Ala Tyr Leu Ile Met Ile Ser Ala Leu Met Ala  
 225 230 235 240  
 Leu Val Phe Ile Lys Tyr Leu Pro Glu Trp Ser Ala Trp Val Ile Leu  
 245 250 255  
 Gly Ala Ile Ser Val Tyr Asp Leu Val Ala Val Leu Cys Pro Lys Gly  
 260 265 270  
 Pro Leu Arg Met Leu Val Glu Thr Ala Gln Glu Arg Asn Glu Pro Ile  
 275 280 285  
 Phe Pro Ala Leu Ile Tyr Ser Ser Ala Met Val Trp Thr Val Gly Met  
 290 295 300  
 Ala Lys Leu Asp Pro Ser Ser Gln Gly Ala Leu Gln Leu Pro Tyr Asp  
 305 310 315 320  
 Pro Glu Met Glu Glu Asp Ser Tyr Asp Ser Phe Gly Glu Pro Ser Tyr  
 325 330 335  
 Pro Glu Val Phe Glu Pro Pro Leu Thr Gly Tyr Pro Gly Glu Glu Leu  
 340 345 350  
 Glu Glu Glu Glu Glu Arg Gly Val Lys Leu Gly Leu Gly Asp Phe Ile  
 355 360 365  
 Phe Tyr Ser Val Leu Val Gly Lys Ala Ala Ala Thr Gly Ser Gly Asp  
 370 375 380  
 Trp Asn Thr Thr Leu Ala Cys Phe Val Ala Ile Leu Ile Gly Leu Cys  
 385 390 395 400  
 Leu Thr Leu Leu Leu Leu Ala Val Phe Lys Lys Ala Leu Pro Ala Leu  
 405 410 415  
 Pro Ile Ser Ile Thr Phe Gly Leu Ile Phe Tyr Phe Ser Thr Asp Asn  
 420 425 430  
 Leu Val Arg Pro Phe Met Asp Thr Leu Ala Ser His Gln Leu Tyr Ile  
 435 440 445

# SEQUENCE LISTING

<110> St. George-Hyslop, Peter H.  
Rommens, Johanna  
Fraser, Paul E.

<120> Alzheimer's Related Proteins and Methods  
of Use

<130> 1034/1F810-US1

<140> 09/227,725

<141> 1999-01-08

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<170> FastSEQ for Windows Version 3.0

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<211> 467

<212> PRT

<213> Homo Sapien

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| Met | Thr | Glu | Leu | Pro | Ala | Pro | Leu | Ser | Tyr | Phe | Gln | Asn | Ala | Gln | Met |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
| Ser | Glu | Asp | Asn | His | Leu | Ser | Asn | Thr | Val | Arg | Ser | Gln | Asn | Asp | Asn |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
| Arg | Glu | Arg | Gln | Glu | His | Asn | Asp | Arg | Arg | Ser | Leu | Gly | His | Pro | Glu |
|     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
| Pro | Leu | Ser | Asn | Gly | Arg | Pro | Gln | Gly | Asn | Ser | Arg | Gln | Val | Val | Glu |
|     | 50  |     |     |     |     | 55  |     |     |     | 60  |     |     |     |     |     |
| Gln | Asp | Glu | Glu | Glu | Asp | Glu | Glu | Leu | Thr | Leu | Lys | Tyr | Gly | Ala | Lys |
| 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
| His | Val | Ile | Met | Leu | Phe | Val | Pro | Val | Thr | Leu | Cys | Met | Val | Val | Val |
|     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
| Val | Ala | Thr | Ile | Lys | Ser | Val | Ser | Phe | Tyr | Thr | Arg | Lys | Asp | Gly | Gln |
|     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
| Leu | Ile | Tyr | Thr | Pro | Phe | Thr | Glu | Asp | Thr | Glu | Thr | Val | Gly | Gln | Arg |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
| Ala | Leu | His | Ser | Ile | Leu | Asn | Ala | Ala | Ile | Met | Ile | Ser | Val | Ile | Val |
|     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
| Val | Met | Thr | Ile | Leu | Leu | Val | Val | Leu | Tyr | Lys | Tyr | Arg | Cys | Tyr | Lys |
| 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
| Val | Ile | His | Ala | Trp | Leu | Ile | Ile | Ser | Ser | Leu | Leu | Leu | Leu | Phe | Phe |
|     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
| Phe | Ser | Phe | Ile | Tyr | Leu | Gly | Glu | Val | Phe | Lys | Thr | Tyr | Asn | Val | Ala |
|     |     |     | 180 |     |     |     | 185 |     |     |     |     |     | 190 |     |     |
| Val | Asp | Tyr | Ile | Thr | Val | Ala | Leu | Leu | Ile | Trp | Asn | Phe | Gly | Val | Val |
|     |     | 195 |     |     |     |     | 200 |     |     |     | 205 |     |     |     |     |
| Gly | Met | Ile | Ser | Ile | His | Trp | Lys | Gly | Pro | Leu | Arg | Leu | Gln | Gln | Ala |
|     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
| Tyr | Leu | Ile | Met | Ile | Ser | Ala | Leu | Met | Ala | Leu | Val | Phe | Ile | Lys | Tyr |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     | 240 |
| Leu | Pro | Glu | Trp | Thr | Ala | Trp | Leu | Ile | Leu | Ala | Val | Ile | Ser | Val |
|     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |
| Asp | Leu | Val | Ala | Val | Leu | Cys | Pro | Lys | Gly | Pro | Leu | Arg | Met | Leu |
|     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |
| Glu | Thr | Ala | Gln | Glu | Arg | Asn | Glu | Thr | Leu | Phe | Pro | Ala | Leu | Ile |
|     |     | 275 |     |     |     |     | 280 |     |     |     | 285 |     |     | Tyr |
| Ser | Ser | Thr | Met | Val | Trp | Leu | Val | Asn | Met | Ala | Glu | Gly | Asp | Pro |
|     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     | Glu |
| Ala | Gln | Arg | Arg | Val | Ser | Lys | Asn | Ser | Lys | Tyr | Asn | Ala | Glu | Ser |
| 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     | Thr |
| Glu | Arg | Glu | Ser | Gln | Asp | Thr | Val | Ala | Glu | Asn | Asp | Asp | Gly | Gly |
|     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |
| Ser | Glu | Glu | Trp | Glu | Ala | Gln | Arg | Asp | Ser | His | Leu | Gly | Pro | His |
|     |     |     | 340 |     |     |     |     | 345 |     |     |     |     | 350 | Arg |
| Ser | Thr | Pro | Glu | Ser | Arg | Ala | Ala | Val | Gln | Glu | Leu | Ser | Ser | Ser |
|     |     | 355 |     |     |     |     | 360 |     |     |     |     | 365 |     | Ile |
| Leu | Ala | Gly | Glu | Asp | Pro | Glu | Glu | Arg | Gly | Val | Lys | Leu | Gly | Leu |
|     | 370 |     |     |     |     | 375 |     |     |     |     | 380 |     |     | Gly |
| Asp | Phe | Ile | Phe | Tyr | Ser | Val | Leu | Val | Gly | Lys | Ala | Ser | Ala | Thr |
| 385 |     |     |     |     | 390 |     |     |     |     | 395 |     |     |     | Ala |
| Ser | Gly | Asp | Trp | Asn | Thr | Thr | Ile | Ala | Cys | Phe | Val | Ala | Ile | Leu |
|     |     |     |     | 405 |     |     |     |     | 410 |     |     |     |     | Ile |
| Gly | Leu | Cys | Leu | Thr | Leu | Leu | Leu | Leu | Ala | Ile | Phe | Lys | Lys | Ala |
|     |     |     | 420 |     |     |     |     | 425 |     |     |     |     | 430 | Leu |
| Pro | Ala | Leu | Pro | Ile | Ser | Ile | Thr | Phe | Gly | Leu | Val | Phe | Tyr | Phe |
|     |     | 435 |     |     |     |     | 440 |     |     |     |     | 445 |     | Ala |
| Thr | Asp | Tyr | Leu | Val | Gln | Pro | Phe | Met | Asp | Gln | Leu | Ala | Phe | His |
|     | 450 |     |     |     |     | 455 |     |     |     |     | 460 |     |     | Gln |
| Phe | Tyr | Ile |     |     |     |     |     |     |     |     |     |     |     |     |
| 465 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |

<210> 2  
 <211> 448  
 <212> PRT  
 <213> Homo Sapien

<400> 2

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Leu | Thr | Phe | Met | Ala | Ser | Asp | Ser | Glu | Glu | Glu | Val | Cys | Asp | Glu |
| 1   |     |     |     | 5   |     |     |     | 10  |     |     |     |     | 15  |     |     |
| Arg | Thr | Ser | Leu | Met | Ser | Ala | Glu | Ser | Pro | Thr | Pro | Arg | Ser | Cys | Gln |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
| Glu | Gly | Arg | Gln | Gly | Pro | Glu | Asp | Gly | Glu | Asn | Thr | Ala | Gln | Trp | Arg |
|     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
| Ser | Gln | Glu | Asn | Glu | Glu | Asp | Gly | Glu | Glu | Asp | Pro | Asp | Arg | Tyr | Val |
|     | 50  |     |     |     |     | 55  |     |     |     | 60  |     |     |     |     |     |
| Cys | Ser | Gly | Val | Pro | Gly | Arg | Pro | Pro | Gly | Leu | Glu | Glu | Glu | Leu | Thr |
| 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     | 80  |     |
| Leu | Lys | Tyr | Gly | Ala | Lys | His | Val | Ile | Met | Leu | Phe | Val | Pro | Val | Thr |
|     |     |     | 85  |     |     |     |     |     | 90  |     |     |     |     | 95  |     |
| Leu | Cys | Met | Ile | Val | Val | Val | Ala | Thr | Ile | Lys | Ser | Val | Arg | Phe | Tyr |
|     |     | 100 |     |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
| Thr | Glu | Lys | Asn | Gly | Gln | Leu | Ile | Tyr | Thr | Pro | Phe | Thr | Glu | Asp | Thr |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Pro | Ser | Val | Gly | Gln | Arg | Leu | Leu | Asn | Ser | Val | Leu | Asn | Thr | Leu | Ile |
|     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
| Met | Ile | Ser | Val | Ile | Val | Val | Met | Thr | Ile | Phe | Leu | Val | Val | Leu | Tyr |
| 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
| Lys | Tyr | Arg | Cys | Tyr | Lys | Phe | Ile | His | Gly | Trp | Leu | Ile | Met | Ser | Ser |
|     |     |     | 165 |     |     |     |     |     | 170 |     |     |     |     | 175 |     |
| Leu | Met | Leu | Leu | Phe | Leu | Phe | Thr | Tyr | Ile | Tyr | Leu | Gly | Glu | Val | Leu |
|     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
| Lys | Thr | Tyr | Asn | Val | Ala | Met | Asp | Tyr | Pro | Thr | Leu | Leu | Leu | Thr | Val |
|     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
| Trp | Asn | Phe | Gly | Ala | Val | Gly | Met | Val | Cys | Ile | His | Trp | Lys | Gly | Pro |
|     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
| Leu | Val | Leu | Gln | Gln | Ala | Tyr | Leu | Ile | Met | Ile | Ser | Ala | Leu | Met | Ala |
| 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
| Leu | Val | Phe | Ile | Lys | Tyr | Leu | Pro | Glu | Trp | Ser | Ala | Trp | Val | Ile | Leu |
|     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
| Gly | Ala | Ile | Ser | Val | Tyr | Asp | Leu | Val | Ala | Val | Leu | Cys | Pro | Lys | Gly |
|     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |
| Pro | Leu | Arg | Met | Leu | Val | Glu | Thr | Ala | Gln | Glu | Arg | Asn | Glu | Pro | Ile |
|     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |
| Phe | Pro | Ala | Leu | Ile | Tyr | Ser | Ser | Ala | Met | Val | Trp | Thr | Val | Gly | Met |
|     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |
| Ala | Lys | Leu | Asp | Pro | Ser | Ser | Gln | Gly | Ala | Leu | Gln | Leu | Pro | Tyr | Asp |
| 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |
| Pro | Glu | Met | Glu | Glu | Asp | Ser | Tyr | Asp | Ser | Phe | Gly | Glu | Pro | Ser | Tyr |
|     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |     |
| Pro | Glu | Val | Phe | Glu | Pro | Pro | Leu | Thr | Gly | Tyr | Pro | Gly | Glu | Glu | Leu |
|     |     |     | 340 |     |     |     |     | 345 |     |     |     |     | 350 |     |     |
| Glu | Glu | Glu | Glu | Glu | Arg | Gly | Val | Lys | Leu | Gly | Leu | Gly | Asp | Phe | Ile |
|     |     | 355 |     |     |     | 360 |     |     |     |     | 365 |     |     |     |     |
| Phe | Tyr | Ser | Val | Leu | Val | Gly | Lys | Ala | Ala | Ala | Thr | Gly | Ser | Gly | Asp |
|     | 370 |     |     |     |     | 375 |     |     |     |     | 380 |     |     |     |     |
| Trp | Asn | Thr | Thr | Leu | Ala | Cys | Phe | Val | Ala | Ile | Leu | Ile | Gly | Leu | Cys |
| 385 |     |     |     |     | 390 |     |     |     |     | 395 |     |     |     |     | 400 |
| Leu | Thr | Leu | Leu | Leu | Leu | Ala | Val | Phe | Lys | Lys | Ala | Leu | Pro | Ala | Leu |
|     |     |     |     | 405 |     |     |     | 410 |     |     |     |     | 415 |     |     |
| Pro | Ile | Ser | Ile | Thr | Phe | Gly | Leu | Ile | Phe | Tyr | Phe | Ser | Thr | Asp | Asn |
|     |     |     | 420 |     |     |     |     | 425 |     |     |     |     | 430 |     |     |
| Leu | Val | Arg | Pro | Phe | Met | Asp | Thr | Leu | Ala | Ser | His | Gln | Leu | Tyr | Ile |
|     |     | 435 |     |     |     |     | 440 |     |     |     |     | 445 |     |     |     |

<210> 3  
 <211> 1084  
 <212> PRT  
 <213> Homo Sapien

<220>  
 <221> UNSURE  
 <222> (115)  
 <223> Xaa can be any amino acid

<400> 3  
 Met Thr Phe Asn Ala Gly Pro Ser Leu Leu Ser Gln Ser Ala Leu Gln  
 1 5 10 15

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| Leu | Asn | Ser | Lys | Pro | Glu | Gly | Ser | Phe | Gln | Tyr | Pro | Ala | Ser | Tyr | His |  |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |  |
| Ser | Asn | Gln | Thr | Leu | Ala | Leu | Glu | Glu | Thr | Thr | Pro | Ser | Gln | Leu | Pro |  |
|     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |  |
| Ala | Arg | Gly | Thr | Gln | Ala | Arg | Ala | Thr | Gly | Gln | Ser | Phe | Ser | Gln | Gly |  |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |  |
| Thr | Thr | Ser | Arg | Ala | Gly | His | Leu | Ala | Gly | Pro | Glu | Pro | Ala | Pro | Pro |  |
| 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |  |
| Pro | Pro | Pro | Pro | Pro | Arg | Glu | Pro | Phe | Ala | Pro | Ser | Leu | Gly | Ser | Ala |  |
|     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |  |
| Phe | His | Leu | Pro | Asp | Ala | Pro | Pro | Ala | Ala | Ala | Ala | Ala | Ala | Leu | Tyr |  |
|     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |  |
| Tyr | Ser | Xaa | Ser | Thr | Leu | Pro | Ala | Pro | Pro | Arg | Gly | Gly | Ser | Pro | Leu |  |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |  |
| Ala | Ala | Pro | Gln | Gly | Gly | Ser | Pro | Thr | Lys | Leu | Gln | Arg | Gly | Gly | Ser |  |
|     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |  |
| Ala | Pro | Glu | Gly | Ala | Thr | Tyr | Ala | Ala | Pro | Arg | Gly | Ser | Ser | Pro | Lys |  |
| 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |  |
| Gln | Ser | Pro | Ser | Arg | Leu | Ala | Lys | Ser | Tyr | Ser | Thr | Ser | Ser | Pro | Ile |  |
|     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |  |
| Asn | Ile | Val | Val | Ser | Ser | Ala | Gly | Leu | Ser | Pro | Ile | Arg | Val | Thr | Ser |  |
|     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |  |
| Pro | Pro | Thr | Val | Gln | Ser | Thr | Ile | Ser | Ser | Ser | Pro | Ile | His | Gln | Leu |  |
|     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |  |
| Ser | Ser | Thr | Ile | Gly | Thr | Tyr | Ala | Thr | Leu | Ser | Pro | Thr | Lys | Arg | Leu |  |
|     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |  |
| Val | His | Ala | Ser | Glu | Gln | Tyr | Ser | Lys | His | Ser | Gln | Glu | Leu | Tyr | Ala |  |
| 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |  |
| Thr | Ala | Thr | Leu | Gln | Arg | Pro | Gly | Ser | Leu | Ala | Ala | Gly | Ser | Arg | Ala |  |
|     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |  |
| Ser | Tyr | Ser | Ser | Gln | His | Gly | His | Leu | Gly | Pro | Glu | Leu | Arg | Ala | Leu |  |
|     |     | 260 |     |     |     |     |     | 265 |     |     |     |     | 270 |     |     |  |
| Gln | Ser | Pro | Glu | His | His | Ile | Asp | Pro | Ile | Tyr | Glu | Asp | Arg | Val | Tyr |  |
|     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |  |
| Gln | Lys | Pro | Pro | Met | Arg | Ser | Leu | Ser | Gln | Ser | Gln | Gly | Asp | Pro | Leu |  |
|     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |  |
| Pro | Pro | Ala | His | Thr | Gly | Thr | Tyr | Arg | Thr | Ser | Thr | Ala | Pro | Ser | Ser |  |
| 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |  |
| Pro | Gly | Val | Asp | Ser | Val | Pro | Leu | Gln | Arg | Thr | Gly | Ser | Gln | His | Gly |  |
|     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |  |
| Pro | Gln | Asn | Ala | Ala | Ala | Ala | Thr | Phe | Gln | Arg | Ala | Ser | Tyr | Ala | Ala |  |
|     |     | 340 |     |     |     |     |     | 345 |     |     |     |     | 350 |     |     |  |
| Gly | Pro | Ala | Ser | Asn | Tyr | Ala | Asp | Pro | Tyr | Arg | Gln | Leu | Gln | Tyr | Cys |  |
|     |     | 355 |     |     |     |     | 360 |     |     |     |     | 365 |     |     |     |  |
| Pro | Ser | Val | Glu | Ser | Pro | Tyr | Ser | Lys | Ser | Gly | Pro | Ala | Leu | Pro | Pro |  |
|     | 370 |     |     |     |     | 375 |     |     |     |     | 380 |     |     |     |     |  |
| Glu | Gly | Thr | Leu | Ala | Arg | Ser | Pro | Ser | Ile | Asp | Ser | Ile | Gln | Lys | Asp |  |
| 385 |     |     |     |     | 390 |     |     |     |     | 395 |     |     |     |     | 400 |  |
| Pro | Arg | Glu | Phe | Gly | Trp | Arg | Asp | Pro | Glu | Leu | Pro | Glu | Val | Ile | Gln |  |
|     |     |     |     | 405 |     |     |     |     | 410 |     |     |     |     | 415 |     |  |
| Met | Leu | Gln | His | Gln | Phe | Pro | Ser | Val | Gln | Ser | Asn | Ala | Ala | Ala | Tyr |  |
|     |     |     | 420 |     |     |     |     | 425 |     |     |     |     | 430 |     |     |  |
| Leu | Gln | His | Leu | Cys | Phe | Gly | Asp | Asn | Lys | Ile | Lys | Ala | Glu | Ile | Arg |  |
|     |     | 435 |     |     |     |     | 440 |     |     |     |     |     | 445 |     |     |  |



|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Arg | Gln | Gly | Gly | Ile | Gln | Leu | Leu | Val | Asp | Leu | Leu | Asp | His | Arg | Met |
| 450 |     |     |     |     |     | 455 |     |     |     |     | 460 |     |     |     |     |
| Thr | Glu | Val | His | Arg | Ser | Ala | Cys | Gly | Ala | Leu | Arg | Asn | Leu | Val | Tyr |
| 465 |     |     |     |     | 470 |     |     |     |     | 475 |     |     |     |     | 480 |
| Gly | Lys | Ala | Asn | Asp | Asp | Asn | Lys | Ile | Ala | Leu | Lys | Asn | Cys | Gly | Gly |
|     |     |     |     | 485 |     |     |     |     | 490 |     |     |     |     | 495 |     |
| Ile | Pro | Ala | Leu | Val | Arg | Leu | Leu | Arg | Lys | Thr | Thr | Asp | Leu | Glu | Ile |
|     |     |     | 500 |     |     |     |     | 505 |     |     |     |     | 510 |     |     |
| Arg | Glu | Leu | Val | Thr | Gly | Val | Leu | Trp | Asn | Leu | Ser | Ser | Cys | Asp | Ala |
|     |     | 515 |     |     |     |     | 520 |     |     |     |     | 525 |     |     |     |
| Leu | Lys | Met | Pro | Ile | Ile | Gln | Asp | Ala | Leu | Ala | Val | Leu | Thr | Asn | Ala |
|     | 530 |     |     |     |     | 535 |     |     |     |     | 540 |     |     |     |     |
| Val | Ile | Ile | Pro | His | Ser | Gly | Trp | Glu | Asn | Ser | Pro | Leu | Gln | Asp | Asp |
| 545 |     |     |     |     | 550 |     |     |     |     | 555 |     |     |     |     | 560 |
| Arg | Lys | Ile | Gln | Leu | His | Ser | Ser | Gln | Val | Leu | Arg | Asn | Ala | Thr | Gly |
|     |     |     |     | 565 |     |     |     |     | 570 |     |     |     |     | 575 |     |
| Cys | Leu | Arg | Asn | Val | Ser | Ser | Ala | Gly | Glu | Glu | Ala | Arg | Arg | Arg | Met |
|     |     |     | 580 |     |     |     |     | 585 |     |     |     |     | 590 |     |     |
| Arg | Glu | Cys | Asp | Gly | Leu | Thr | Asp | Ala | Leu | Leu | Tyr | Val | Ile | Gln | Ser |
|     |     | 595 |     |     |     |     | 600 |     |     |     |     | 605 |     |     |     |
| Ala | Leu | Gly | Ser | Ser | Glu | Ile | Asp | Ser | Lys | Thr | Val | Glu | Asn | Cys | Val |
|     | 610 |     |     |     |     | 615 |     |     |     |     | 620 |     |     |     |     |
| Cys | Ile | Leu | Arg | Asn | Leu | Ser | Tyr | Arg | Leu | Ala | Ala | Glu | Thr | Ser | Gln |
| 625 |     |     |     |     | 630 |     |     |     |     | 635 |     |     |     |     | 640 |
| Gly | Gln | His | Met | Gly | Thr | Asp | Glu | Leu | Asp | Gly | Leu | Leu | Cys | Gly | Glu |
|     |     |     |     | 645 |     |     |     |     | 650 |     |     |     |     | 655 |     |
| Ala | Asn | Gly | Lys | Asp | Ala | Glu | Ser | Ser | Gly | Cys | Trp | Gly | Lys | Lys | Lys |
|     |     |     | 660 |     |     |     |     | 665 |     |     |     |     | 670 |     |     |
| Lys | Lys | Lys | Lys | Ser | Gln | Asp | Gln | Trp | Asp | Gly | Val | Gly | Pro | Leu | Pro |
|     |     | 675 |     |     |     |     | 680 |     |     |     |     | 685 |     |     |     |
| Asp | Cys | Ala | Glu | Pro | Pro | Lys | Gly | Ile | Gln | Met | Leu | Trp | His | Pro | Ser |
|     | 690 |     |     |     |     | 695 |     |     |     |     | 700 |     |     |     |     |
| Ile | Val | Lys | Pro | Tyr | Leu | Thr | Leu | Leu | Ser | Glu | Cys | Ser | Asn | Pro | Asp |
| 705 |     |     |     |     | 710 |     |     |     |     | 715 |     |     |     |     | 720 |
| Thr | Leu | Glu | Gly | Ala | Ala | Gly | Ala | Leu | Gln | Asn | Leu | Ala | Ala | Gly | Ser |
|     |     |     |     | 725 |     |     |     |     | 730 |     |     |     |     | 735 |     |
| Trp | Lys | Trp | Ser | Val | Tyr | Ile | Arg | Ala | Ala | Val | Arg | Lys | Glu | Lys | Gly |
|     |     |     | 740 |     |     |     |     | 745 |     |     |     |     | 750 |     |     |
| Leu | Pro | Ile | Leu | Val | Glu | Leu | Leu | Arg | Ile | Asp | Asn | Asp | Arg | Val | Val |
|     |     | 755 |     |     |     |     | 760 |     |     |     |     | 765 |     |     |     |
| Cys | Ala | Val | Ala | Thr | Ala | Leu | Arg | Asn | Met | Ala | Leu | Asp | Val | Arg | Asn |
|     | 770 |     |     |     |     | 775 |     |     |     |     | 780 |     |     |     |     |
| Lys | Glu | Leu | Ile | Gly | Lys | Tyr | Ala | Met | Arg | Asp | Leu | Val | His | Arg | Leu |
| 785 |     |     |     |     | 790 |     |     |     |     | 795 |     |     |     |     | 800 |
| Pro | Gly | Gly | Asn | Asn | Ser | Asn | Asn | Thr | Ala | Ser | Lys | Ala | Met | Ser | Asp |
|     |     |     | 805 |     |     |     |     |     | 810 |     |     |     |     | 815 |     |
| Asp | Thr | Val | Thr | Ala | Val | Cys | Cys | Thr | Leu | His | Glu | Val | Ile | Thr | Lys |
|     |     |     | 820 |     |     |     |     | 825 |     |     |     |     | 830 |     |     |
| Asn | Met | Glu | Asn | Ala | Lys | Ala | Leu | Arg | Asp | Ala | Gly | Gly | Ile | Glu | Lys |
|     |     | 835 |     |     |     |     | 840 |     |     |     |     | 845 |     |     |     |
| Leu | Val | Gly | Ile | Ser | Lys | Ser | Lys | Gly | Asp | Lys | His | Ser | Pro | Lys | Val |
|     | 850 |     |     |     |     | 855 |     |     |     |     | 860 |     |     |     |     |
| Val | Lys | Ala | Ala | Ser | Gln | Val | Leu | Asn | Ser | Met | Trp | Gln | Tyr | Arg | Asp |
| 865 |     |     |     |     | 870 |     |     |     |     | 875 |     |     |     |     | 880 |

|      |      |      |      |      |      |      |      |     |      |      |      |      |      |      |      |
|------|------|------|------|------|------|------|------|-----|------|------|------|------|------|------|------|
| Leu  | Arg  | Ser  | Leu  | Tyr  | Lys  | Lys  | Asp  | Gly | Trp  | Ser  | Gln  | Tyr  | His  | Phe  | Val  |
|      |      |      |      | 885  |      |      |      |     | 890  |      |      |      |      | 895  |      |
| Ala  | Ser  | Ser  | Ser  | Thr  | Ile  | Glu  | Arg  | Asp | Arg  | Gln  | Arg  | Pro  | Tyr  | Ser  | Ser  |
|      |      |      | 900  |      |      |      |      | 905 |      |      |      |      | 910  |      |      |
| Ser  | Arg  | Thr  | Pro  | Ser  | Ile  | Ser  | Pro  | Val | Arg  | Val  | Ser  | Pro  | Asn  | Asn  | Arg  |
|      |      | 915  |      |      |      |      | 920  |     |      |      |      | 925  |      |      |      |
| Ser  | Ala  | Ser  | Ala  | Pro  | Ala  | Ser  | Pro  | Arg | Glu  | Met  | Ile  | Ser  | Leu  | Lys  | Glu  |
|      | 930  |      |      |      |      | 935  |      |     |      |      | 940  |      |      |      |      |
| Arg  | Lys  | Thr  | Asp  | Tyr  | Glu  | Cys  | Thr  | Gly | Ser  | Asn  | Ala  | Thr  | Tyr  | His  | Gly  |
| 945  |      |      |      |      | 950  |      |      |     |      | 955  |      |      |      |      | 960  |
| Gly  | Lys  | Gly  | Glu  | His  | Thr  | Ser  | Arg  | Lys | Asp  | Ala  | Met  | Thr  | Ala  | Gln  | Asn  |
|      |      |      |      | 965  |      |      |      |     | 970  |      |      |      |      | 975  |      |
| Thr  | Gly  | Ile  | Ser  | Thr  | Leu  | Tyr  | Arg  | Asn | Ser  | Tyr  | Gly  | Ala  | Pro  | Ala  | Glu  |
|      |      |      | 980  |      |      |      |      | 985 |      |      |      |      | 990  |      |      |
| Asp  | Ile  | Lys  | His  | Asn  | Gln  | Val  | Ser  | Ala | Gln  | Pro  | Val  | Pro  | Gln  | Glu  | Pro  |
|      |      | 995  |      |      |      |      | 1000 |     |      |      |      | 1005 |      |      |      |
| Ser  | Arg  | Lys  | Asp  | Tyr  | Glu  | Thr  | Tyr  | Gln | Pro  | Phe  | Gln  | Asn  | Ser  | Thr  | Arg  |
|      | 1010 |      |      |      |      | 1015 |      |     |      |      | 1020 |      |      |      |      |
| Asn  | Tyr  | Asp  | Glu  | Ser  | Phe  | Phe  | Glu  | Asp | Gln  | Val  | His  | His  | Arg  | Pro  | Pro  |
| 1025 |      |      |      |      | 1030 |      |      |     |      | 1035 |      |      |      |      | 1040 |
| Ala  | Ser  | Glu  | Tyr  | Thr  | Met  | His  | Leu  | Gly | Leu  | Lys  | Ser  | Thr  | Gly  | Asn  | Tyr  |
|      |      |      |      | 1045 |      |      |      |     | 1050 |      |      |      |      | 1055 |      |
| Val  | Asp  | Phe  | Tyr  | Ser  | Ala  | Ala  | Arg  | Pro | Tyr  | Ser  | Glu  | Leu  | Asn  | Tyr  | Glu  |
|      |      |      | 1060 |      |      |      | 1065 |     |      |      |      |      | 1070 |      |      |
| Thr  | Ser  | His  | Tyr  | Pro  | Ala  | Ser  | Pro  | Asp | Ser  | Trp  | Val  |      |      |      |      |
|      |      | 1075 |      |      |      |      | 1080 |     |      |      |      |      |      |      |      |

<210> 4

<211> 1193

<212> PRT

<213> Homo Sapien

<400> 4

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Pro | Ala | Pro | Glu | Gln | Ala | Ser | Leu | Val | Glu | Glu | Gly | Gln | Pro | Gln |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
| Thr | Arg | Gln | Glu | Ala | Ala | Ser | Thr | Gly | Pro | Cys | Met | Glu | Pro | Glu | Thr |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
| Thr | Ala | Thr | Thr | Ile | Leu | Ala | Ser | Val | Lys | Glu | Gln | Glu | Leu | Gln | Phe |
|     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
| Gln | Arg | Leu | Thr | Arg | Glu | Leu | Glu | Val | Glu | Arg | Gln | Ile | Val | Ala | Ser |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
| Gln | Leu | Glu | Arg | Cys | Arg | Leu | Gly | Ala | Glu | Ser | Pro | Ser | Ile | Ala | Ser |
| 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
| Thr | Ser | Ser | Thr | Glu | Lys | Ser | Phe | Pro | Trp | Arg | Ser | Thr | Asp | Val | Pro |
|     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
| Asn | Thr | Gly | Val | Ser | Lys | Pro | Arg | Val | Ser | Asp | Ala | Val | Gln | Pro | Asn |
|     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
| Asn | Tyr | Leu | Ile | Arg | Thr | Glu | Pro | Glu | Gln | Gly | Thr | Leu | Tyr | Ser | Pro |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
| Glu | Gln | Thr | Ser | Leu | His | Glu | Ser | Glu | Gly | Ser | Leu | Gly | Asn | Ser | Arg |
|     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
| Ser | Ser | Thr | Gln | Met | Asn | Ser | Tyr | Ser | Asp | Ser | Gly | Tyr | Gln | Glu | Ala |
| 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Cys | Ser | Phe | His | Asn | Ser | Gln | Asn | Val | Ser | Lys | Ala | Asp | Asn | Arg | Gln |
|     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
| Gln | His | Ser | Phe | Ile | Gly | Ser | Thr | Asn | Asn | His | Val | Val | Arg | Asn | Ser |
|     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
| Arg | Ala | Glu | Gly | Gln | Thr | Leu | Val | Gln | Pro | Ser | Val | Ala | Asn | Arg | Ala |
|     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
| Met | Arg | Arg | Val | Ser | Ser | Val | Pro | Ser | Arg | Ala | Gln | Ser | Pro | Ser | Tyr |
|     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
| Val | Ile | Ser | Thr | Gly | Val | Ser | Pro | Ser | Arg | Gly | Ser | Leu | Arg | Thr | Ser |
| 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
| Leu | Gly | Ser | Gly | Phe | Gly | Ser | Pro | Ser | Val | Thr | Asp | Pro | Arg | Pro | Leu |
|     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
| Asn | Pro | Ser | Ala | Tyr | Ser | Ser | Thr | Thr | Leu | Pro | Ala | Ala | Arg | Ala | Ala |
|     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |
| Ser | Pro | Tyr | Arg | Ser | Gln | Arg | Pro | Ala | Ser | Pro | Thr | Ala | Ile | Arg | Arg |
|     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |
| Ile | Gly | Ser | Val | Thr | Ser | Arg | Gln | Thr | Ser | Asn | Pro | Asn | Gly | Pro | Thr |
|     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |
| Pro | Gln | Tyr | Gln | Thr | Thr | Ala | Arg | Val | Gly | Ser | Pro | Leu | Thr | Leu | Thr |
| 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |
| Asp | Ala | Gln | Thr | Arg | Val | Ala | Ser | Pro | Ser | Gln | Gly | Gln | Val | Cys | Ser |
|     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |
| Ser | Ser | Pro | Lys | Arg | Ser | Gly | Met | Thr | Ala | Val | Pro | Gln | His | Leu | Gly |
|     |     |     | 340 |     |     |     |     | 345 |     |     |     |     | 350 |     |     |
| Pro | Ser | Leu | Gln | Arg | Thr | Val | His | Asp | Met | Glu | Gln | Phe | Cys | Gln | Gln |
|     |     | 355 |     |     |     |     | 360 |     |     |     |     | 365 |     |     |     |
| Gln | Tyr | Asp | Ile | Tyr | Glu | Arg | Met | Val | Pro | Pro | Arg | Pro | Asp | Ser | Leu |
|     | 370 |     |     |     |     | 375 |     |     |     |     | 380 |     |     |     |     |
| Thr | Cys | Leu | Arg | Ser | Ser | Tyr | Ala | Ser | Gln | His | Ser | Gln | Leu | Gly | Gln |
| 385 |     |     |     |     | 390 |     |     |     |     | 395 |     |     |     |     | 400 |
| Asp | Ile | Arg | Ser | Ala | Val | Ser | Pro | Asp | Leu | His | Ile | Thr | Pro | Ile | Tyr |
|     |     |     |     | 405 |     |     |     | 410 |     |     |     |     |     | 415 |     |
| Glu | Cys | Arg | Thr | Tyr | Tyr | Tyr | Ser | Pro | Val | Tyr | Arg | Ser | Pro | Asn | His |
|     |     |     | 420 |     |     |     |     | 425 |     |     |     |     | 430 |     |     |
| Cys | Ile | Val | Glu | Leu | Gln | Gly | Ser | Gln | Thr | Ala | Leu | Tyr | Arg | Thr | Cys |
|     |     | 435 |     |     |     |     | 440 |     |     |     |     | 445 |     |     |     |
| Val | Glu | Gly | Ile | Gly | Asn | Leu | Gln | Arg | Thr | Ser | Ser | Gln | Arg | Ser | Thr |
|     | 450 |     |     |     |     | 455 |     |     |     |     |     | 460 |     |     |     |
| Leu | Thr | Tyr | Gln | Arg | Asn | Asn | Tyr | Ala | Leu | Asn | Thr | Thr | Ala | Thr | Tyr |
| 465 |     |     |     |     | 470 |     |     |     |     | 475 |     |     |     |     | 480 |
| Ala | Glu | Pro | Tyr | Arg | Pro | Ile | Gln | Tyr | Arg | Val | Gln | Glu | Cys | Asn | Tyr |
|     |     |     |     | 485 |     |     |     |     | 490 |     |     |     |     | 495 |     |
| Asn | Arg | Leu | Gln | His | Ala | Val | Pro | Ala | Asp | Asp | Gly | Thr | Thr | Arg | Ser |
|     |     |     | 500 |     |     |     |     | 505 |     |     |     |     | 510 |     |     |
| Pro | Ser | Ile | Asp | Ser | Ile | Gln | Lys | Asp | Pro | Arg | Glu | Phe | Ala | Trp | Arg |
|     |     | 515 |     |     |     |     | 520 |     |     |     |     | 525 |     |     |     |
| Asp | Pro | Glu | Leu | Pro | Glu | Val | Ile | His | Met | Leu | Glu | His | Gln | Phe | Phe |
|     | 530 |     |     |     |     | 535 |     |     |     |     | 540 |     |     |     |     |
| Ser | Val | Gln | Ala | Asn | Ala | Ala | Tyr | Leu | Gln | His | Ile | Cys | Phe | Gly |     |
| 545 |     |     |     |     | 550 |     |     |     | 555 |     |     |     |     | 560 |     |
| Asp | Asn | Lys | Val | Lys | Met | Glu | Val | Cys | Arg | Leu | Cys | Gly | Ile | Lys | His |
|     |     |     |     | 565 |     |     |     |     | 570 |     |     |     |     | 575 |     |
| Leu | Val | Asp | Leu | Leu | Asp | His | Arg | Val | Leu | Glu | Val | Gln | Lys | Asn | Ala |
|     |     |     | 580 |     |     |     |     | 585 |     |     |     |     | 590 |     |     |

|     |      |     |     |     |     |      |      |     |     |     |     |      |     |     |     |  |
|-----|------|-----|-----|-----|-----|------|------|-----|-----|-----|-----|------|-----|-----|-----|--|
| Cys | Gly  | Ala | Leu | Arg | Asn | Leu  | Val  | Phe | Gly | Lys | Ser | Thr  | Asp | Glu | Asn |  |
|     |      | 595 |     |     |     |      | 600  |     |     |     |     | 605  |     |     |     |  |
| Lys | Ile  | Ala | Met | Lys | Asn | Val  | Gly  | Gly | Ile | Phe | Ala | Leu  | Leu | Arg | Ile |  |
|     | 610  |     |     |     |     | 615  |      |     |     |     | 620 |      |     |     |     |  |
| Ile | Arg  | Lys | Ser | Ile | Asp | Ala  | Glu  | Val | Arg | Glu | Ile | Val  | Thr | Gly | Val |  |
| 625 |      |     |     |     | 630 |      |      |     |     | 635 |     |      |     |     | 640 |  |
| Leu | Trp  | Asn | Leu | Ser | Ser | Cys  | Asp  | Ala | Val | Lys | Met | Thr  | Ile | Ile | Arg |  |
|     |      |     |     | 645 |     |      |      |     | 650 |     |     |      |     | 655 |     |  |
| Asp | Ala  | Leu | Ser | Thr | Leu | Thr  | Asn  | Thr | Val | Ile | Val | Pro  | His | Ser | Cys |  |
|     |      |     | 660 |     |     |      |      | 665 |     |     |     |      | 670 |     |     |  |
| Trp | Asn  | Asn | Ser | Ser | Phe | Asp  | Asp  | Asp | His | Lys | Ile | Lys  | Phe | Gln | Thr |  |
|     |      | 675 |     |     |     |      | 680  |     |     |     |     | 685  |     |     |     |  |
| Ser | Leu  | Val | Leu | Arg | Asn | Thr  | Thr  | Gly | Cys | Leu | Arg | Asn  | Leu | Thr | Ser |  |
|     | 690  |     |     |     |     | 695  |      |     |     |     | 700 |      |     |     |     |  |
| Ala | Gly  | Glu | Phe | Ala | Arg | Lys  | Gln  | Met | Arg | Ser | Cys | Glu  | Gly | Leu | Val |  |
| 705 |      |     |     |     | 710 |      |      |     |     | 715 |     |      |     |     | 720 |  |
| Asp | Ser  | Leu | Leu | Tyr | Val | Ile  | His  | Thr | Cys | Val | Asn | Thr  | Ser | Asp | Tyr |  |
|     |      |     |     | 725 |     |      |      |     | 730 |     |     |      |     | 735 |     |  |
| Asp | Ser  | Lys | Thr | Val | Glu | Asn  | Cys  | Val | Cys | Thr | Leu | Arg  | Asn | Leu | Ser |  |
|     |      |     | 740 |     |     |      |      | 745 |     |     |     |      | 750 |     |     |  |
| Tyr | Arg  | Leu | Glu | Leu | Glu | Val  | Pro  | Gln | Ala | Arg | Leu | Leu  | Gly | Leu | Asn |  |
|     |      | 755 |     |     |     |      | 760  |     |     |     |     | 765  |     |     |     |  |
| Glu | Leu  | Asp | Asp | Leu | Leu | Gly  | Lys  | Glu | Ser | Pro | Ser | Lys  | Asp | Ser | Glu |  |
|     | 770  |     |     |     |     | 775  |      |     |     |     | 780 |      |     |     |     |  |
| Pro | Ser  | Cys | Trp | Gly | Lys | Lys  | Lys  | Lys | Lys | Lys | Lys | Arg  | Thr | Pro | Gln |  |
| 785 |      |     |     |     | 790 |      |      |     |     |     | 795 |      |     |     | 800 |  |
| Pro | Gln  | Glu | Asp | Gln | Trp | Asp  | Cys  | Val | Gly | Pro | Ile | Pro  | Gly | Leu | Ser |  |
|     |      |     |     | 805 |     |      |      |     | 810 |     |     |      |     | 815 |     |  |
| Lys | Ser  | Pro | Lys | Gly | Val | Glu  | Met  | Leu | Trp | His | Pro | Ser  | Val | Val | Lys |  |
|     |      |     | 820 |     |     |      |      | 825 |     |     |     |      | 830 |     |     |  |
| Pro | Tyr  | Leu | Thr | Leu | Leu | Ala  | Glu  | Ser | Ser | Asn | Pro | Ala  | Thr | Leu | Glu |  |
|     |      | 835 |     |     |     |      | 840  |     |     |     |     | 845  |     |     |     |  |
| Cys | Ser  | Ala | Cys | Ser | Leu | Gln  | Asn  | Leu | Ser | Ala | Ser | Asn  | Trp | Lys | Phe |  |
|     |      | 850 |     |     |     | 855  |      |     |     |     | 860 |      |     |     |     |  |
| Ala | Ala  | Tyr | Ile | Arg | Gly | Gly  | Arg  | Pro | Lys | Arg | Lys | Cys  | Leu | Pro | Ile |  |
| 865 |      |     |     |     | 870 |      |      |     |     | 875 |     |      |     |     | 880 |  |
| Leu | Val  | Glu | Leu | Leu | Arg | Met  | Asp  | Asn | Asp | Arg | Val | Val  | Ser | Ser | Cys |  |
|     |      |     |     | 885 |     |      |      |     | 890 |     |     |      |     | 895 |     |  |
| Ala | Thr  | Ala | Leu | Arg | Asn | Met  | Ala  | Leu | Asp | Val | Asn | Lys  | Glu | Leu | Ile |  |
|     |      |     | 900 |     |     |      |      | 905 |     |     |     |      | 910 |     |     |  |
| Cys | Lys  | Tyr | Ala | Met | Arg | Asp  | Leu  | Val | Asn | Arg | Leu | Pro  | Cys | Cys | Asn |  |
|     |      | 915 |     |     |     |      | 920  |     |     |     |     | 925  |     |     |     |  |
| Gly | Pro  | Ser | Val | Leu | Ser | Asp  | Glu  | Thr | Met | Ala | Ala | Ile  | Cys | Cys | Ala |  |
|     | 930  |     |     |     |     | 935  |      |     |     |     | 940 |      |     |     |     |  |
| Leu | His  | Glu | Val | Thr | Ser | Lys  | Asn  | Met | Glu | Asn | Ala | Lys  | Ala | Leu | Ala |  |
| 945 |      |     |     |     | 950 |      |      |     |     | 955 |     |      |     |     | 960 |  |
| Asp | Ser  | Gly | Gly | Ile | Glu | Lys  | Leu  | Val | Asn | Ile | Thr | Lys  | Gly | Arg | Gly |  |
|     |      |     |     | 965 |     |      |      |     | 970 |     |     |      |     | 975 |     |  |
| Asp | Arg  | Ser | Ser | Leu | Lys | Val  | Val  | Lys | Ala | Ala | Ala | Gln  | Val | Leu | Asn |  |
|     |      |     | 980 |     |     |      |      | 985 |     |     |     |      | 990 |     |     |  |
| Thr | Leu  | Trp | Gln | Tyr | Arg | Asp  | Leu  | Arg | Ser | Ile | Tyr | Lys  | Lys | Asp | Gly |  |
|     |      | 995 |     |     |     |      | 1000 |     |     |     |     | 1005 |     |     |     |  |
| Trp | Asn  | His | Pro | Ile | Thr | Pro  | Val  | Ser | Thr | Leu | Glu | Arg  | Asp | Arg | Phe |  |
|     | 1010 |     |     |     |     | 1015 |      |     |     |     |     | 1020 |     |     |     |  |

[illegible]